Crystal Structure of the Self-Complementary 5′-Purine Start Decamer d(GCGCGCGCGC) in the Z-DNA Conformation. I

Changill Ban, Boopathy Ramakrishnan, and Muttaiya Sundaralingam
Laboratory of Biological Macromolecular Structure, Departments of Chemistry and Biochemistry and The Ohio State Biochemistry Program, The Ohio State University, Columbus, Ohio 43210 USA

ABSTRACT Alternating self-complementary oligonucleotides starting with a 5′-pyrimidine usually form left-handed Z-DNA; however, with a 5′-purine start sequence they form the right-handed A-DNA. Here we report the crystal structure of the decamer d(GCGCGCGCGC) with a 5′-purine start in the Z-DNA form. The decamer crystallizes in the hexagonal space group $P6_522$, unit cell dimensions $a = b = 18.08$ and $c = 43.10$ Å, with one of the following four dinucleotide diphosphates in the asymmetric unit: d(pGpC)/d(GpCp)/d(pCpG)/d(CpGp). The molecular replacement method, starting with d(pGpC) of the isomorphous Z-DNA hexamer d(araC-dG)$_3$ without the 2′-OH group of arabinose, was used in the structure analysis. The method gave the solution only after the sugar-phosphate conformation of the GpC step was manipulated. The refinement converged to a final R value of 18.6% for 340 unique reflections in the resolution range 8.0–1.9 Å. A result of the sequence alternation is the alternation in the nucleotide conformation; guanosine is C3′-*endo*, *syn*, and cytidine is C2′-*endo*, *anti*. The CpG step phosphodiester conformation is the same as Z_I or Z_{II}, whereas that of the GpC step phosphodiester is "intermediate"in the sense that ζ (O3′-P bond) is the same as Z_{II} but α (P-O5′ bond) is the same as Z_I. The duplexes generated from the dinucleotide asymmetric unit are stacked one on top of the other in the crystal to form an infinite pseudocontinuous helix. This renders it a quasi-polymerlike structure that has assumed the Z-DNA conformation further strengthened by the long inner Z-forming stretch d(CG)$_4$. An interesting feature of the structure is the presence of water strings in both the major and the minor grooves. In the minor groove the cytosine carbonyl oxygen atoms of the GpC and CpG steps are cross-bridged by water molecules that are not themselves hydrogen bonded but are enclosed by the water rings in the mouth of the minor groove. In the major groove three independent water molecules form a zigzagging continuous water string that runs throughout the duplex.

INTRODUCTION

The left-handed Z-DNA is adopted by alternating self-complementary oligonucleotides starting with a 5′-pyrimidine (Wang et al., 1979, 1984; Drew et al., 1980). The only exception is the crystal structure of d(CGCATATATGCG) (Yoon et al., 1988). There are some sequences in which the alternation is disrupted by double pyrimidine/purine, which also has a left-handed structure (Table 1). However, so far all the known 5′-purine start sequences have crystallized as right-handed A-DNA (Jain et al., 1987; Table 1). Apparently the 5′-terminal base type, purine/pyrimidine, has an influence on the stacking and handedness of the short alternating oligonucleotides (Quadrifoglio et al., 1984; Jain et al., 1987). Besides this terminal base effect on the helix handedness, we are interested in the effect of the length of the inner sequence. We selected the all-G·C alternating self-complementary decamer sequence d(GCGCGCGCGC) with a 5′-guanine start and a long inner alternating sequence d(CG)$_4$, which could yield either a left- or a right-handed structure or a mixed-handed right-left junction. Indeed, we were surprised that the decamer assumed the left-handed Z-DNA structure (Figs. 1 and 2), which represents the first self-complementary oligonucleotide with a 5′-purine start in this conformation.

Received for publication 16 January 1996 and in final form 31 May 1996.

Address reprint requests to Dr. Muttaiya Sundaralingam, Laboratory of Biological Macromolecular Structure, Department of Chemistry and Biochemistry, 012 Rightmire Hall, The Ohio State University, 1060 Carmack Road, Columbus, OH 43210. Tel.: 614-292-2925; Fax: 614-292-2524; E-mail: sunda@biot.mps.ohio-state.edu.

0006-3495/96/09/1215/07 $2.00

MATERIALS AND METHODS

Synthesis of the oligonucleotide

We synthesized the alternating decamer d(GCGCGCGCGC) by the phosphotriester method, using an in-house Applied Biosystem DNA synthesizer (ABI-386). The decamer was cleaved from the solid support with 3 ml of 33% ammonia and was deprotected in the same solution at 55°C for 12 h. The oligonucleotide was then precipitated by ethanol in the presence of 2.5 M ammonium acetate at −25°C. The precipitate was dissolved, and the lyophilized decamer solution was used for crystallization without further purification.

Crystallization and data collection

The best crystals of d(GCGCGCGCGC) were obtained with the hanging-drop vapor diffusion method in the presence of 1 mM decamer (single strand), 20 mM sodium cacodylate buffer (pH 7.0), 5 mM magnesium chloride, 0.5 mM spermine tetrachloride, and 5% (v/v) 2-methyl-2,4-pentanediol against a reservoir of 45% 2-methyl-2,4-pentanediol. A crystal of uniform dimensions 0.1 × 0.1 × 0.1 mm, which was grown over a two-month period at room temperature, was mounted for data collection. The crystal belonged to the hexagonal space group $P6_522$, with unit cell dimensions of $a = b = 18.08$ and $c = 43.10$ Å, which were virtually identical to the cell constants of the Z-DNA decamer d(CGTACGTACG) with a different hexagonal space group $P6_5$ (Brennan et al., 1986) but

TABLE 1 Crystal structures of alternating oligonucleotide sequences starting with 5′-pyrimidine and 5′-purine

Sequence	DNA Type	Reference
Pyrimidine start		
CGCG	Z-DNA	Drew et al. (1980)
CGCGCG	Z-DNA	Wang et al. (1979)
CACGTG	Z-DNA	Coll et al. (1988)
CGCGTG	Z-DNA	Ho et al. (1985)
CGATCG*	Z-DNA	Wang et al. (1984)
(mCGGGmCG) · (mCGCCmCG)*	Z-DNA	Schroth et al. (1993)
CGCATGCG	Z-DNA	Fujii et al. (1985)
CGCGCGCG	Z-DNA	Fujii et al. (1985)
CGCICICG	Z-DNA	Kumar et al. (1992)
CGTACGTACG	Z-DNA	Brennan et al. (1986)
CGCATATATGCG	B-DNA	Yoon et al. (1988)
Purine start		
GTGTACAC	A-DNA	Jain et al. (1987)
GTACGTAC	A-DNA	Takusagawa (1990)
ATGCGCAT	A-DNA	Clark et al. (1990)
GTACGTAC	A-DNA	Langlois et al. (1993)
GTGCGCAC	A-DNA	Bingman et al. (1992b)
GCGTACGTACGC	A-DNA	Bingman et al. (1992a)
GsCGsCGsC	B-DNA	Cruse et al. (1986)
GCGCGCGCGC	**Z-DNA**	**This work**

*Nonalternating sequence.

isomorphous to the Z-DNA hexamer d(araC-G)$_3$ in the space group P6$_5$22 (Zhang et al., 1992).

Three-dimensional x-ray intensity data out to 1.9-Å resolution were collected on the crystal at room temperature by the Siemens-Nicolet area detector containing a four-circle goniometer, with a MaxScience rotating anode source operated at 50 kV and 90 mA and a graphite monochromater to select Cu-Kα radiation. The crystal-to-detector distance was 12 cm. A 180° ϕ-scan at χ = 0°and a 75° ω-scan at ϕ = 90°, χ = 45° were performed in 0.25° steps with an exposure time of 60 s/diffraction frame. A total of 1020 frames was collected and processed by the program XENGEN 2.0 (Howard, 1990). Of the 2020 reflections collected, 401 were unique, with R_{symm} = 2.2%. The structure analysis was carried out with 340 unique reflections with $F \geq \sigma(F)$ in the resolution range 8.0–1.9 Å.

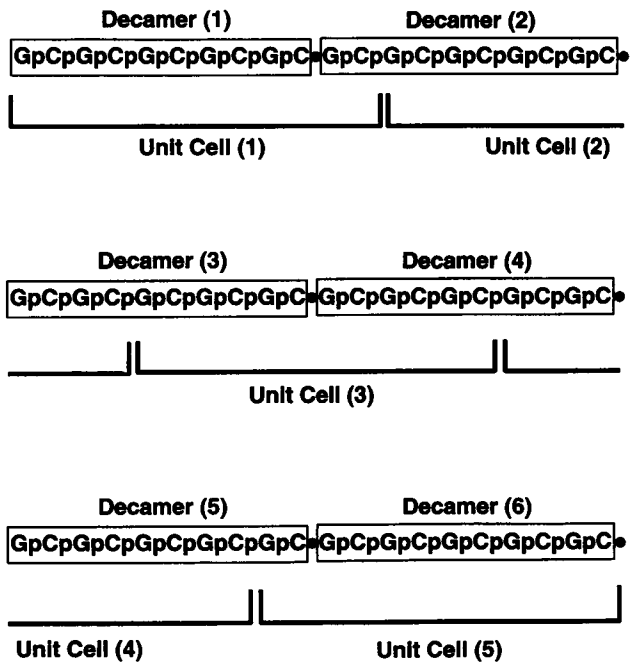

FIGURE 1 Packing relationship of the Z-DNA decamer d(GCGCGCGCGC) (*boxes*) in the unit cell. Unit cell *c*, 43.01 Å long, is along the helix axis of the decamer and can contain a maximum of 12 nucleotide base pairs. This means that six decamers span five unit cells as in Brennan's structure (Brennan et al., 1986). Because the electron density of the ten phosphates, the nine phosphates of the decamer helix, and the junction phosphate (●) is the same, the weight of the phosphate is the same, 9/10.

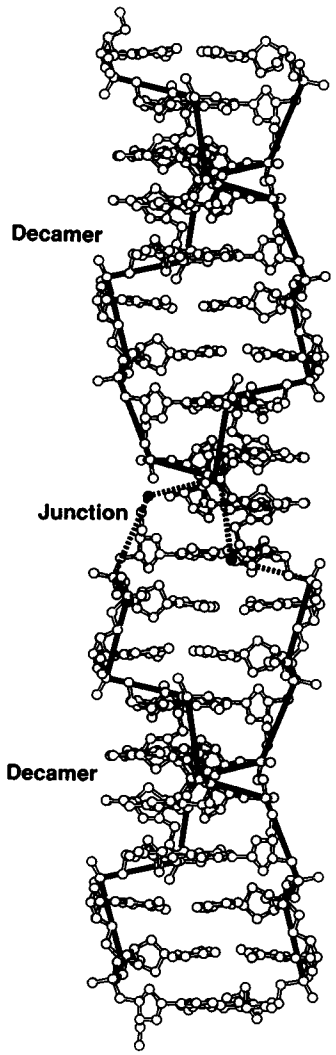

FIGURE 2 Pseudocontinuous helix of the stacked decamer d(GCGCGCGCGC) duplexes, viewed along the molecular dyad of the bottom decamer. The solid dark lines connect the phosphate groups, and the junction phosphates (●) are connected by dashed lines.

Structure solution and refinement

The model chosen for the asymmetry unit of the dinucleotide was d(pGpC) from the isomorphous Z-DNA hexamer (araC-dG)$_3$ (Zhang et al., 1992) without the arabinose O$_2$′-hydroxyl group. An initial rigid-body search with this model failed to yield the structure. Several trials of a manually adjusted model of the sugar-phosphate backbone conformation and position yielded the correct electron density, similar to that of the trial model. A rigid-body refinement by the XPLOR program (Brünger, 1990) that used 60 reflections for 10–2.5-Å resolution dropped the *R* value from 41.0% to

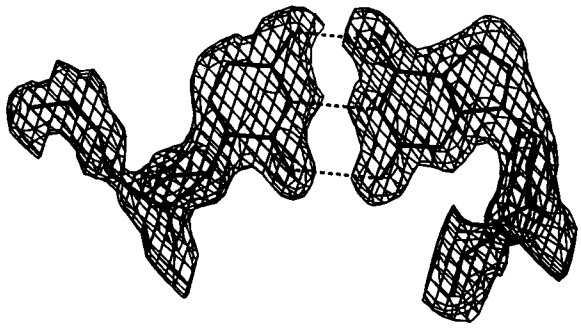

FIGURE 3 3Fo-2Fc electron density map contoured at 1σ, showing clearly the ordered density for the G·C base pairs of the dinucleotide repeat of the decamer d(GCGCGCGCGC). The guanosine is *syn* and C3′-*endo*, and the cytidine is *anti* and C2′-*endo*.

33.7%. To maintain the geometry for the internucleotide phosphate linkage between the terminal guanosine and cytosine residues we included two "dummy" residues with zero occupancies flanking the dinucleotide repeat unit (see also Zhang et al., 1992). Further refinement was carried out with 340 reflections in the range 8.0–1.9 Å, which dropped the R value to 29.8%. The standard omit maps that leave out the entire base from the dinucleotide repeating unit could not be calculated because this base is a large fraction (20–25%) of the scattering mass. So we calculated omit maps by omitting five or six base atoms at a time and the phosphate and sugar atoms. This confirmed the model with the *syn* conformation for guanosine and the *anti* conformation for cytidine (Fig. 3). The model was then annealed at 1200°C and slowly cooled to 300°C with a 0.5-fs sampling interval, giving an R value of 25.3%. The rms deviation from the starting model was 1.1 Å. Most of this difference came from the conformational difference of the GpC phosphate. Further fitting to 3Fo-2Fc and Fo-Fc difference electron density maps and refinement confirmed that the GpC phosphate conformation (Fig. 4*b*) was different from the known values of Z-DNA. The electron densities for the bases and sugars are ordered (Fig. 3).

The continuous backbone density suggests the presence of a phosphate group at the junction between the stacked decamer helices. The junction (3′-C-5′-G) phosphate has the same weight as do the other phosphates of the CpG steps within the decamer helix. Thus, the phosphate group of the CpG step is statistically disordered throughout the crystal, with a density of 9/10 of a normal phosphate (Fig. 4 *a*). The decamer d(GCGCGCGCGC) was modeled from the dinucleotide asymmetry unit d(pGpC) by applica-

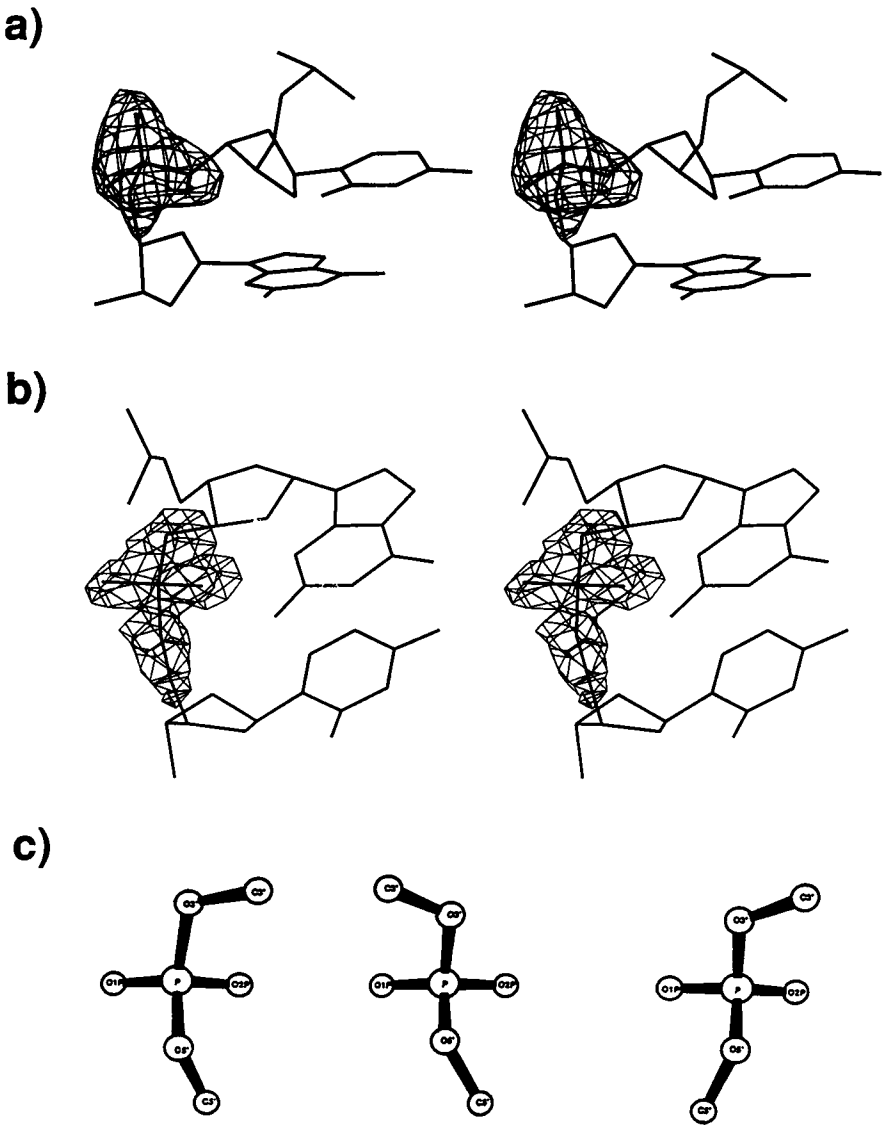

FIGURE 4 (*a*) Fo-Fc electron density map, omitting the phosphate group and the C5′ atom of the CpG step, contoured at 2.5σ. (*b*) Fo-Fc electron density map, omitting the phosphate group and the C5′ atom of the GpC step. The novel GpC phosphodiester conformation is illustrated in (*c*). (*c*) d(GpC) step ($Z_{I/II}$) phosphate conformation (left) compared with the corresponding steps of the major Z_I (middle) and minor Z_{II} (right) conformations in Z-DNA. The GpC guanosine ζ (O3′-P) torsion (+*gauche* or +*synclinal*) is similar to Z_{II}, while the cytosine α (P-O5′) torsion (*trans* or −*anticlinal*) is similar to Z_I.

TABLE 2 Crystal and refinement parameters of the Z-DNA decamer d(GCGCGCGCGC)

Unit cell dimensions (Å)	
$a = b$	18.08
c	43.10
Space group	$P6_522$ Hexagonal
Molecule/asymmetric unit cell	d(pGpC) or d(GpCp)/d(pCpG) or d(CpGp)
Data completeness (%) in ∞–1.9 Å	96.4 (378/392)
Number of reflections ($F \geq \sigma(F)$) used in refinement in resolution range 8.0–1.9 Å	340
Final R value (%)	18.6
RMS deviation from ideal geometry	
Parameter file used	param11.dna
Bond lengths (Å)	0.012
Bond angles (°)	3.3
Dihedral angles (°)	31.0
"Improper" angles (°)	3.4
Final model	
Nucleic acid atoms	41
Water molecules	14
Average thermal parameter (Å^2)	
Nucleotide	19
Water molecules	66

tion of the crystallographic twofold axes normal to the helix axis and passing through the center of adjacent base pairs (Fig. 2).

Solvent molecules identified from omit difference maps were incorporated into the model during the refinement. There was no cation in the model. The final R value is 18.6% for a structure containing 41 nucleotide atoms and 14 water molecules. The crystallographic refinement parameters are listed in Table 2. The atomic coordinates will be deposited with the Nucleic Acid Database (Berman et al., 1992).

RESULTS

Overall structure

The decamer duplex forms a pseudocontinuous stacked column along the c axis. Six duplexes complete five unit cells, similar to the Z-DNA decamer d(CGTACGTACG) (Brennan et al., 1986) (Figs. 1 and 2). However, unlike the latter Z-DNA decamer, the nucleoside bases and sugars of the repeating unit here are ordered (Fig. 3). The CpG phosphodiester has the Z_I or Z_{II} conformation (Table 3), whereas the GpC phosphodiester (ζ = 56° and α = -140°) is different (Fig. 4 *b*); the cytosine α (*trans*/(−)*anticlinal*) is the same as Z_I, but the guanine ζ (+*gauche*/(+)*synclinal*) is the same as Z_{II} (Table 3; Fig. 4 *c*). The rms deviation of the sugar-phosphate backbone atoms of the present GpC step is 1.5 Å from Z_I and 1.2 Å from Z_{II}, indicating that the conformational alternation of the phosphate torsions in the present structure is different from those of other Z-DNA.

The widths of the minor groove (8.7 Å) and the convex major groove (15.1 Å) are comparable with the other Z-DNA values (Wang et al., 1979; Drew et al., 1980). As in Z-DNA, the cytidine is C2′-*endo*, *anti*, whereas the guanosine is C3′-*endo*, *syn*. The global helix parameters (NEWHEL92, R.E. Dickerson, personal communication) are typical of Z-DNA, notwithstanding the fact that the GpC phosphate is different. The average base pair rise is 3.6 Å. The twist of the CpG step is 10.2°, and the GpC step is 49.8°, with an overall twist of 60.0°. The roll angles also alternate, with opposite signs for the GpC steps (−7.2°) and the CpG steps (7.3°). The alternation is not significant in the slide, inclination, x-displacement, tilt, and buckle angles. The propeller twist is uniform, 3.2°.

TABLE 3 Comparison of sugar-phosphate backbone torsions* and pseudorotation phase angles (*P*) of the present decamer d(GCGCGCGCGC) with the idealized Z_I and Z_{II} conformations

	d(GCGCGCGCGC) (This work)		Z_I (Wang et al., 1981)		Z_{II} (Wang et al., 1981)	
	G	C	G	C	G	C
α	60°	**−140°**	47°	−137°	92°	146°
β	−164	−175	179	−139	−167	164
γ	−176	5	−165	56	157	66
δ	84	161	99	138	94	147
ϵ	−174	−88	−104	−94	−179	−100
ζ	**56**	70	−69	80	55	74
χ	57	−127	68	−159	62	−148
P	58	176	−3	152	50	163

*The backbone torsion angles as defined by IUPAC-IUB (1983) are O3′-*P*-α-O5′-β-C5′-γ-C4′-δ-C3′-ϵ-O3′-ζ-P-O5′.

Stacking at the CpG and GpC steps

The base stacking overlap within the duplex is similar to those of the other Z-DNAs. At the CpG step compared with the GpC step the bases are poorly stacked but are compensated by the sugar-base stacking, giving a probable reason why pyrimidine start oligonucleotides can readily form Z-DNA whereas purine start sequences do not (Jain et al., 1987). However, irrespective of the starting base, the polymers $d(CG)_n$ and $d(GC)_n$ usually form Z-DNA, where $n \rightarrow \infty$ and py/pu $\approx$ 1. The present Z-DNA decamer d(GCGCGCGCGC) seems to mimic poly-d(GC). This is possible because the 6_522 helix symmetry of Z-DNA can be readily accommodated in a crystal lattice with the helix axis coinciding with the crystallographic symmetry, which indicates that Z-DNA oligonucleotides, like the present decamer, can form quasi-polymers in single crystals. However, the 11_1 helix symmetry of A-DNA fibers and the 10_1 helix symmetry of B-DNA fibers are not permitted for single crystals.

Hydration: water string and rings

Each dinucleotide repeat unit d(pGpC) is associated with 14 water molecules (Table 4). Eleven water molecules are directly hydrogen bonded to the dinucleotide (first shell), and the remaining three are in the second sphere. The structure displays some interesting patterns of water network. There are three independent water molecules in the major groove. One (W5) bridges guanine carbonyl O6 atoms of the GpC steps, and a second (W3) bridges cytosine amino N4 atoms of the CpG steps (Fig. 5 *a*);

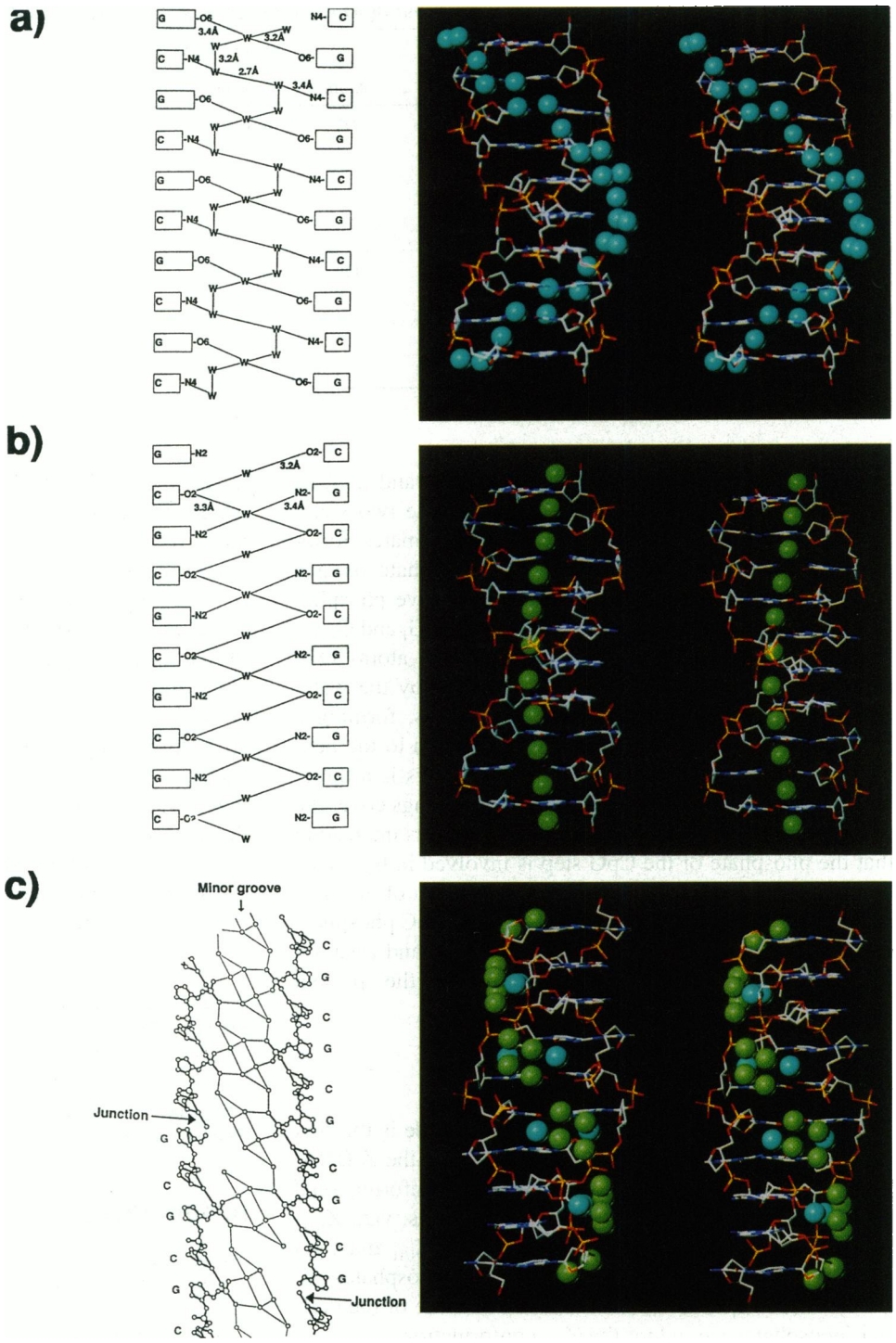

FIGURE 5 Schematic illustrations (*left*) and stereo views (*right*) of the water strings in the major and minor grooves and the water rings in the mouth of the minor groove. In the stereo views the molecule is rendered as balls and sticks; the water molecules are shown as spheres. (*a*) In the major groove GpC step, the guanine O6 atoms on both strands are cross-linked by a water molecule, and the cytosine N4 atoms of the CpG step on both strands are bridged by two water molecules. The stereo view shows the continuous water string in the major groove, which runs through the entire duplex in the left-handed topology. (*b*) In the minor groove CpG step,the O_2 atoms of the cytosine residues and the N2 atoms of the guanine residues are water bridged. In the GpC step only the O_2 atoms of cytosine residues are water bridged, but the waters themselves are too far apart (3.7 Å) to be hydrogen bonded. These bridges are nearly along the helix axis of the duplex. (*c*) A cylindrical projection, showing the minor groove of the helices (calculated at a radius of 10 Å and an angular range of 360°), with the water rings. The closest minor groove phosphorus–phosphorus distance of 8.7 Å is between the G_i residue (strand 1) and the twofold related $G_{i'+3}$ residue (strand 2). The phosphate anionic oxygen O_2P atoms of the G_i residue and the $G_{i'+3}$ residue are bridged by two water molecules to form a hexagonal ring (four waters and two anionic oxygen atoms). The next closest phosphorus–phosphorus separation (10.3 Å) is between G_i and $G_{i'+5}$. Here, O1P of G_i and O_2P of $G_{i'+5}$ are again bridged by two water molecules, which form a four-membered water ring. The lack of phosphate groups at the junction results in an incomplete hexagonal ring. The minor groove water rings at the mouth envelop the water bridges (string) inside the minor groove.

such water bridges are common features in Z-DNA (Gessner et al., 1994). But in the present structure an additional water (W16) bridges the first two water molecules to form a continuous zigzagging water string $(W3\cdots W16\cdots W5\cdots W3\cdots)_n$ in the major groove (Fig. 5 *a*). This novel left-handed water string seems further to stabilize the helix.

In the minor groove the O_2 atoms of the cytosine bases of the GpC and CpG steps in the two strands are cross-bridged by the water molecules W10 and W12, which themselves are not hydrogen bonded, to form a quasi-continuous water "string" (Fig. 5 *b*), as found by Chevrier et al. (1986) and Gessner et al. (1994). In addition, the two amino groups of the guanines in the CpG steps may also form hydrogen bonding/electrostactic interactions with W10 (Table 4; Fig. 5 *b*).

Some of the phosphates lining the minor groove are found to be involved in a striking hydration scheme. The closest minor groove phosphorus–phosphorus separation of

TABLE 4 Hydration of the dinucleotide repeat unit d(pGpC) in the Z-DNA decamer d(GCGCGCGCGC)

	Major groove sites			Minor groove sites			Backbone sites		
Residue	Atom	Water	Distance (Å)	Atom	Water	Distance (Å)	Atom	Water	Distance (Å)
G	O6	W5	3.4	N2	W10	3.4	O3′	W14	2.7
		W7	3.4				O1P	W8	3.3
								W9	3.1
							O2P	W6	3.1
								W11	2.9
								W15	3.4
C	N4	W3	3.4	O2	W10	3.3	O5′	W14	2.9
					W12	3.2	O1P	W3	3.0
								W14	2.4
							O2P	W7	2.6
								W11	2.7

8.7 Å is between G_i (strand 1) and $G_{i'+3}$ (strand 2). The CpG steps across the groove are linked by the two water molecules, W8 and W9, and their dyad-related mates, forming a hexagonal ring with the anionic phosphate oxygen atoms (Fig. 5 *c*). The next closest minor groove phosphorus–phosphorus distance of 10.3 Å is between G_i and $G_{i'+5}$. Here, both anionic phosphate anionic oxygen atoms O1P and O_2P of the same CpG step are hydrated by the water molecules W6 and W8 and their dyad mates, forming a four-membered water ring (Fig. 5 *c*). Common to the hexagonal ring and the four-membered water rings is a three-membered water ring. These repeating water rings cover the mouth of the entire minor groove (Fig. 5 *c*). It is interesting that the phosphate of the CpG step is involved in hydrogen bonding to the water ring network, whereas that of the GpC step is not. This might be the reason why the GpC phosphate exhibits greater flexibility than the CpG step and assumes the intermediate (Z_I/Z_{II}) conformation in the present structure.

DISCUSSION

The present 10-nucleotides-long oligonucleotide is the first example of a 5′-purine start duplex exhibiting the Z-DNA. This Z-DNA is significantly different in the conformational alternation for the backbone phosphate torsions, viz., $Z_{I/II}$-Z_I-$Z_{I/II}$-Z_I-$Z_{I/II}$-Z_I-$Z_{I/II}$-Z_I-$Z_{I/II}$, where GpC is $Z_{I/II}$ and CpG is Z_I. In the known Z-DNAs the CpG step phosphates are always in the Z_I conformation and one or more of the GpC step phosphates can adopt the Z_{II} conformation.

The preference for Z-DNA with a 5′-pyrimidine start has been rationalized in terms of the greater stacking stability of the n CpG steps compared with the $n - 1$ GpC steps (Jain et al., 1987). Indeed, the polynucleotides $d(CG)_n$ and $d(GC)_n$, regardless of the starting base, are left-handed in high salt concentration (Arnott et al., 1980). This is because the ratio of the py-pu to the pu-py steps is near unity. However, in purine start oligonucleotides, where there are n GpC steps and $n - 1$ CpG steps, they tend to be right-handed. Circular dichroism studies of $d(GC)_n$ (n = 3–7) corroborate this observation; in high salt they are right-handed, and when the sequence is reversed they are left-handed (Quadrifoglio et al., 1984). When $n \geq 5$ the oligonucleotides show a weak tendency for the left-handed conformation, whereas the octamer (n = 4) and the hexamer (n = 3) show no tendency for Z-DNA and a stronger tendency for the right-handed structure. Also, methylation of the octamer and the hexamer stabilizes the A-DNA conformation in crystals (Mooers et al., 1995). The present decamer structure probably forms a Z-DNA because it has an optimal length for the inner stretch $d(CG)_4$ and also stacks to form an infinite continuous polymerlike structure, poly $d(GC)_n$/poly $d(CG)_n$. The above factors contribute to the Z-DNA formation in the crystal, in contrast to the right-handed conformation in solution (Quadrifoglio et al., 1984). Thus, in crystals the decamer $d(GC)_5$ overrides the effect of the purine base start.

We thank the National Institutes of Health for grant GM-17378 and the Regents of Ohio for an Ohio Eminent Scholar Chair to M.S. We also thank the Ohio State Supercomputer Center for a grant of computer time on the Cray Y-MP/864 computer.

This paper was presented at the Ninth Conversation in Biomolecular Stereodynamics, Albany, NY, 20–24 June 1995, abstract 007.

REFERENCES

Arnott, S., R. Chandrasekaran, D. L. Birdsall, A. G. W. Leslie, and R. L. Ratliff. 1980. Left-handed DNA helices. *Nature (Lond.).* 283:743–745.

Berman, H. M., W. K. Olson, D. Beveridge, J. Westbrook, A. Gelbin, T. Demeny, S. Hsieh, A. R. Srinivasan, and B. Schneider. 1992. The Nucleic Acid Database: a comprehensive relational database of three dimensional structures of nucleic acids. *Biophys. J.* 63:751–759.

Bingman, C., S. Jain, G. Zon, and M. Sundaralingam. 1992a. Crystal and molecular structure of the alternating dodecamer d(GCGTACGTACGC) in the A-DNA form: comparison with the isomorphous non-alternating dodecamer d(CCGTACGTACGG). *Nucleic Acids Res.* 20:6637–6647.

Bingman, C., X. Li, G. Zon, and M. Sundaralingam. 1992b. Crystal and molecular structure of d(GTGCGCAC): investigation of the effects of base sequence on the conformation of octamer duplexes. *Biochemistry.* 31:12,803–12,812.

Brennan, R. G., E. Westhof, and M. Sundaralingam. 1986. Structure of a Z-DNA with two different backbone chain conformations. Stabilization of the decadeoxy oligonucleotide d(CGTACGTACG) by $(Co(NH_3)_6)^{3+}$ binding to the guanine. *J. Biomol. Struct. Dyn.* 3:649–665.

Brünger, A. T. 1990. XPLOR Manual, v2.1. Yale University, New Haven, CT.

Chevrier, B., A. C. Dock, B. Hartmann, M. Leng, D. Moras, M. T. Thuong, and E. Westhof. 1986. Solvation of the left-handed hexamer d(5BrC-G-5BrC-G-5BrC-G) in crystals grown at two temperatures. *J. Mol. Biol.* 188:707–719.

Clark, G. R., D. G. Brown, M. R. Sanderson, T. Chwalinski, S. Neidle, J. M. Veal, R. L. Jones, W. D. Wilson, G. Zon, E. Garman, and D. I. Stuart. 1990. Crystal and solution structures of the oligonucleotide $d(ATGCGCAT)_2$: a combined x-ray and NMR study. *Nucleic Acids Res.* 18:5521–5528.

Coll, M., I. Fita, J. Lloveras, J. A. Subirana, F. Bardella, T. Huynh-Dinh, and J. Igolen. 1988. Structure of d(CACGTG), Z-DNA hexamer containing A·T base pairs. *Nucleic Acids Res.* 16:8695–8705.

Cruse, W. B. T., S. A. Salisbury, T. Brown, R. Cosstick, F. Eckstein, and O. Kennard. 1986. Chiral phosphorothioate analogues of B-DNA: the crystal structure of Rp-d(Gp(S)CpGp(S)CpGp(S)C). *J. Mol. Biol.* 192: 891–905.

Drew, H., T. Takano, K. Itakura, and R. E. Dickerson. 1980. High-salt d(CpGpCpG), a left-handed Z' DNA double helix. *Nature (Lond.).* 286:567–573.

Fujii, S., A. H. -J. Wang, G. J. Quigley, H. Westerink, G. A. van der Marel, J. H. van Boom, and A. Rich. 1985. The octamers d(CGCGCGCG) and d(CGCATGCG) both crystallize as Z-DNA in the same hexagonal lattice. *Biopolymers.* 24:243–250.

Gessner, R. V., G. J. Quigley, and M. Egli. 1994. Comparative studies of high resolution Z-DNA crystal structures. Part 1: Common hydration patterns of alternating dC-dG. *J. Mol. Biol.* 236:1154–1168.

Ho, P. S., C. A. Frederick, G. J. Quigley, G. A. van der Marel, J. H. van Boom, A. H. -J. Wang, and A. Rich, 1985. GT wobble base-pairing in Z-DNA at 1.0 angstrom atomic resolution: the crystal structure of d(CGCGTG). *EMBO J.* 4:3617–3623.

Howard, A. J. 1990. XENGEN Manual, v2.1. Genex Corp., Gaithersburg, MD.

IUPAC-IUB Joint Commission in Biochemistry Nomenclature. 1983. Abbreviations and symbols for the description of conformations of polynucleotide chains. *Eur. J. Biochem* 131:9–15.

Jain, S. C., G. Zon, and M. Sundaralingam. 1987. The potentially Z-DNA-forming sequence d(GTGTACAC) crystallizes as A-DNA. *J. Mol. Biol.* 197:141–145.

Kumar, V. D., R. W. Harrison, L. C. Andrews, and I. T. Weber. 1992. Crystal structure at 1.5 angstroms resolution of d(CGCICICG), an octanucleotide containing inosine, and its comparison with d(CGCG) and d(CGCGCG) structures. *Biochemistry.* 31:1541–1550.

Langlois, D. B., A. Dautant, C. Courseille, and G. Precigoux. 1993. Orthorhombic crystal structure of the A-DNA octamer d(GTACGTAC). Comparison with the tetragonal structure. *Eur. J. Biochem.* 213: 673–682.

Mooers, B. H. M., G. P. Schroth, W. W. Baxter, and P. S. Ho. 1995. Alternating and non-alternating dG-dC hexanucleotides crystallize as canonical A-DNA. *J. Mol. Biol.* 249:772–784.

Quadrifoglio, F., G. Manzini, and N. Yathindra. 1984. Short oligodeoxynucleotides with d(G-C)*n* sequence do not assume left-handed conformation in high salt conditions. *J. Mol. Biol.* 175:419–423.

Saenger, M. 1988. Principles of Nucleic Acid Structure. Springer-Verlag, New York. 283–297.

Schroth, G. P., T. F. Kagawa, and P. S. Ho. 1993. Structure and thermodynamics of nonalternating C·G base pairs in Z-DNA: the 1.3 Å crystal structure of the asymmetric hexanucleotide d(m5CGGGm5CG)·d(m5CGCCm5CG). *Biochemistry.* 32:13,381–13,392.

Takusagawa, T. 1990. The crystal structure of d(GTACGTAC) at 2.25 angstroms resolution. Are the A-DNA's always unwound approximately 10 degrees at the C-G steps? *J. Biomol. Struct. Dyn.* 7:795–809.

Wang, A. H.-J., T. Hakoshima, G. A. van der Marel, J. H. van Boom, and A. Rich. 1984. AT base pairs are less stable than GC base pairs in Z-DNA: the crystal structure of d(m(5)CGTAm(5)CG). *Cell.* 37: 321–331.

Wang, A. H.-J., G. J. Quigley, F. J. Kolpak, J. L. Crawford, J. H. van Boom, G. A. van der Marel, and A. Rich, 1979. Molecular structure of a left-handed double helical DNA fragment at atomic resolution. *Nature (Lond.).* 282:680–686.

Wang, A. H.-J., G. A. van der Marel, R. V. Gessner, and A. Rich, 1981. Left-handed double helical DNA: variations in the backbone conformation. *Nature (Lond.).* 211:171–176.

Yoon, C., G. G. Prive, D. S. Goodsell, and R. E. Dickerson. 1988. Structure of an alternating-B DNA helix and its relationship to A-tract DNA. *Proc. Natl. Acad. Sci. USA.* 85:6332–6336.

Zhang, H., G. A. van der Marel, J. H. van Boom, and A. H. -J. Wang. 1992. Conformational perturbation of the anticancer nucleoside arabinosylcytosine on Z-DNA: molecular structure of $(araC\text{-}dG)_3$ at 1.3 angstroms resolution. *Biopolymer.* 32:1559–1569.